

 comprises asialoGM1 or asialoGM2.--

REMARKS

Claims 1-33 are presently pending in this case. In this preliminary amendment, Applicants have canceled Claim 30, without prejudice, amended Claims 1-29 and 31-33, and added new Claims 34-35. Support for amended Claims 1-29, 31-33, as well as new Claims 34-35, can be found generally throughout the instant Specification, particularly in Claims 1-33 as filed in the priority document. Consequently, the instant Amendment introduces no new matter into the instant Application. Attached hereto is a marked-up version of the changes made to the Claims by the instant Amendment. The attached page is captioned **"Version With Markings To Show Changes Made."**

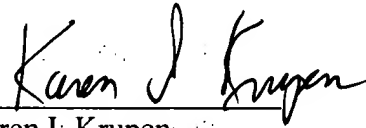
Fees

No fees are believed to be necessitated by the instant response. However, should this be in error, authorization is hereby given to charge Deposit Account no. 18-1982 for any underpayment, or to credit any overpayments.

CONCLUSION

Applicants respectfully submit that the Claims as amended are believed to be in condition for allowance. Thus, early and favorable action on the claims is earnestly solicited.

Respectfully submitted,



Karen I. Krupen
Attorney for Applicant(s)
Registration No. 34,647

AVENTIS PHARMACEUTICALS PRODUCTS, INC.

Route 202-206; Mail Stop: EMC-G1

P.O. Box 6800

Bridgewater, NJ 08807

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Version With Markings To Show Changes Made

1. (Amended) An agent [Agents] for transferring nucleic acids, comprising [characterized in that they comprise] a hydrophobic spacer chemically linked, firstly, to a polycation and, secondly, to at least one hydrophilic substituent.

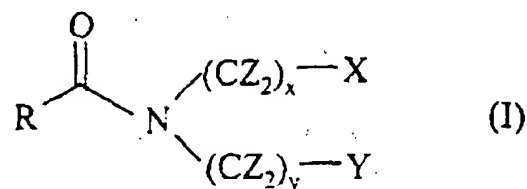
2. (Amended) The agent of Claim 1, [Agents for transferring nucleic acids according to Claim 1, characterized in that] wherein said hydrophobic spacer comprises [consists of 2 or 3] 2 to 3 hydrocarbon-based linear fatty chains comprising between 10 and 20 carbon atoms per chain, wherein said chains need not be of equal length, or a [each chain possibly being of different length, or of said hydrophobic spacer consists of a very long] hydrocarbon-based linear fatty chain comprising between 20 and 50 carbon atoms.

3. (Amended) The agent of Claim 1, wherein said at least one hydrophilic substituent is selected from the group consisting of a hydroxyl substituent, an amino substituent, a polyol, a sugar, and a hydrophilic peptide [Agents for transferring nucleic acids according to Claim 1, characterized in that the hydrophilic substituent(s) is (are) chosen from hydroxyl or amino substituents, polyols, sugars or hydrophilic peptides].

4. (Amended) The agent of Claim 3, wherein said at least one hydrophilic substituent comprises [Agents for transferring nucleic acids according to Claim 1 or 3, characterized in that at least one of the hydrophilic substituents is] a sugar.

5. (Amended) The agent of [Agents for transferring nucleic acids according to]

Claim 1, of general formula (I):

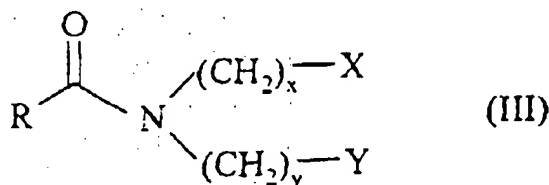


for which:

- R represents a polycation,
- Z represents a hydrogen atom or a fluorine atom, the various Zs being independent of each other, and
- either x and y, independently of each other, represent integers between 10 and 22 inclusive, and X and Y, independently of each other, represent a hydrogen atom, an -OAlk group in which Alk represents a straight or branched alkyl containing 1 to 4 carbon atoms, a hydroxyl group, an amino group, a polyol, a sugar, a hydrophilic or non-hydrophilic peptide, or an oligonucleotide, it being understood that at least one of the X and Y substituents represents a hydrophilic group chosen from hydroxyl groups, amino groups, polyols, sugars or hydrophilic peptides,
- or x is equal to 0 or 1, y is an integer between 20 and 50, X is either a hydrogen atom or an -OAlk group in which Alk represents a straight or branched alkyl containing 1 to 4 carbon atoms, and Y is a hydrophilic group comprising a hydroxyl group, an amino group, a polyol, or a hydrophilic peptide [chosen from hydroxyl groups, amino groups, polyols, sugars or hydrophilic peptides],

where appropriate in the isomeric forms thereof, and also the mixtures thereof or the salts thereof, when they exist.

6. (Amended) The agent of Claim 1 [Agents for transferring nucleic acids according to Claim 1 or 5,] of general formula (III):



for which:

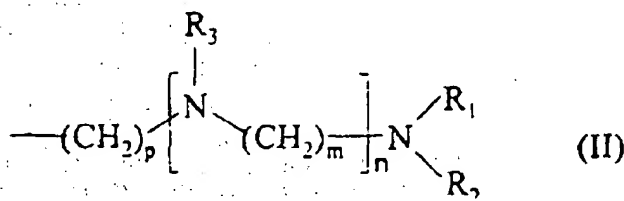
- R represents a polycation, and
- either x and y, independently of each other, represent integers between 10 and 22 inclusive, and X and Y, independently of each other, represent a hydrogen atom or a sugar, it being understood that at least one of the X and Y substituents represents a sugar,
- or x is equal to 0 or 1, y is an integer between 20 and 50, X is a hydrogen atom and Y is a sugar,

where appropriate in the isomeric forms thereof, and also the mixtures thereof or the salts thereof, when they exist.

7. (Amended) The agent of Claim 6, wherein [Agents for transferring nucleic acids according to Claim 6, characterized in that] x and y, independently of each other, represent integers between 10 and 22 inclusive, and one of X and Y represents a hydrogen atom and the other a sugar.

8. (Amended) The agent of Claim 1, wherein [Agents for transferring nucleic acids according to one of Claims 1 and 5 to 7, characterized in that] said polycation is a linear or branched polyamine, each amino group being separated by one or more methylene groups.

9. (Amended) The agent of Claim 8, wherein [Agents for transferring nucleic acids according to Claim 8, characterized in that] said polycation has the general formula (II):



in which:

- R_1 , R_2 and R_3 represent, independently of each other, a hydrogen atom or a $(\text{CH}_2)_q\text{NR}'\text{R}''$ group with q an integer possibly ranging from 1 to 6, this being independent among the various R_1 , R_2 and R_3 groups, it being understood that at least one of R_1 , R_2 and R_3 is other than a hydrogen atom,
- R' and R'' represent, independently of each other, a hydrogen atom or a $(\text{CH}_2)_q\text{NH}_2$ group with q defined as above,
- m represents an integer between 1 and 6, and
- n and p represent, independently of each other, integers between 0 and 6, with, when n is greater than or equal to 2, m being able to have different values and R_3 different meanings within the general formula (II) and, when n is equal to 0, at least one of the R_1

and R₂ substituents is other than a hydrogen atom.

10. (Amended) The agent of Claim 1, wherein said polycation is selected from the group consisting of: [Agents for transferring nucleic acids according to one of Claims 1 and 5 to 7, characterized in that said polycation is chosen from] spermine, spermidine, cadaverine, putrescine, hexamethylenetetramine (hexamine), methacrylamidopropyltrimethylammonium chloride (AMBTAC), 3-acrylamido-3-methylbutyltrimethylammonium chloride (AMBTAC), polyvinylamine, polyethyleneimine, and ionene [polyvinylamines, polyethyleneimines, or ionenes].

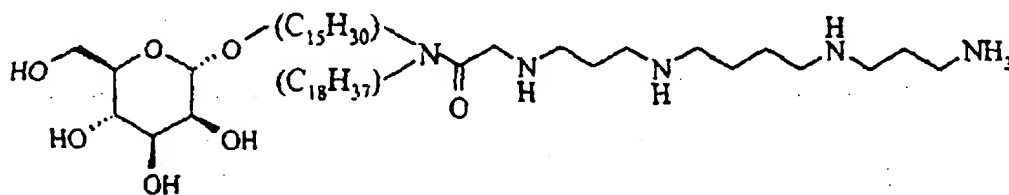
11. (Amended) The agent of Claim 3, wherein said sugar comprises a monosaccharide, an oligosaccharide, or a polysaccharide [Agents for transferring nucleic acids according to one of Claims 3 to 7, characterized in that the sugar(s) is (are) a molecule or molecules of mono-, oligo- or polysaccharide].

12. (Amended) The agent of Claim 11, wherein said sugar comprises [Agents for transferring nucleic acids according to Claim 11, characterized in that said sugar(s) is (are) chosen from] glucose, mannose, rhamnose, galactose, fructose, maltose, lactose, saccharose, sucrose, fucose, cellobiose, allose, laminarabiose, gentiobiose, sophorose, melibiose, dextran, α -amylose, amylopectin, fructan, mannan, xylan, or arabinan [fructans, mannans, xylans and arabinans].

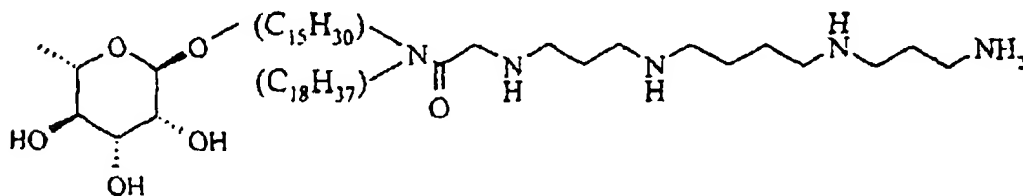
13. (Amended) The agent of Claim 5, wherein [Agents for transferring nucleic acids according to Claim 5, characterized in that] said oligonucleotide is any chain containing one or more nucleotides, deoxynucleotides, ribonucleotides and/or deoxyribonucleotides[, optionally coupled to one or more molecules having distinct properties].

14. (Amended) The agent of Claim 5, wherein [Agents for transferring nucleic acids according to Claim 5, characterized in that] said peptide is any chain containing one or more amino acids linked to each other via attachments of a peptide nature, optionally substituted with one or more aliphatic groups which may be saturated or unsaturated, and linear, branched or cyclic.

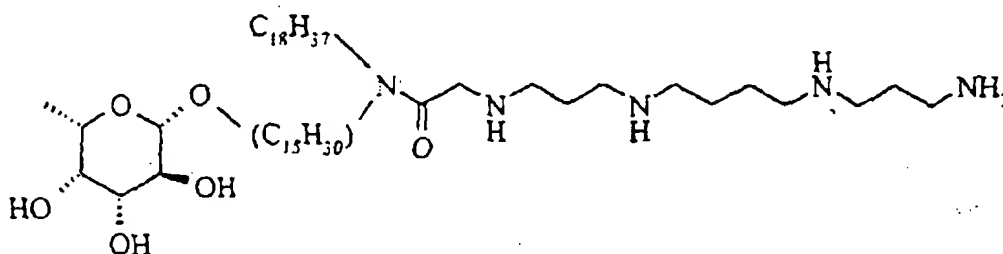
15. (Amended) The agent of Claim 1, having a [Transfer agent according to Claim 1, of] formula:



16. (Amended) The agent of Claim 1, having a [Transfer agent according to Claim 1, of] formula:



17. (Amended) The agent of Claim 1, having a [Transfer agent according to Claim 1, of] formula:



18. (Amended) A composition comprising [Composition characterized in that it contains an] agent of Claim 1 [for transferring nucleic acids as defined in Claims 1 to 17], and a nucleic acid.

19. (Amended) The composition of Claim 18, wherein [Composition according to Claim 18, characterized in that] the nucleic acid is a deoxyribonucleic acid or a ribonucleic acid.

20. (Amended) The composition of Claim 18, wherein [Composition according to Claim 18 or 19, characterized in that] said nucleic acid comprises one or more genes of therapeutic interest under the control of regulatory sequences.

21. (Amended) The composition of Claim 18, wherein [Composition according to Claims 18 to 20, characterized in that] said nucleic acid is an antisense sequence or gene.

22. (Amended) The composition of Claim 18, further comprising an adjuvant [Composition according to Claim 18, characterized in that it also contains one or more

adjuvants].

23. (Amended) The composition of Claim 22, wherein [Composition according to Claim 22, characterized in that] the adjuvant is a neutral lipid [one or more neutral lipids].

24. (Amended) The composition of Claim 23, wherein said neutral lipid
comprises [Composition according to Claim 23, characterized in that the neutral lipids are lipids containing] two fatty chains.

25. (Amended) The composition of Claim 23, wherein said neutral lipid is a
natural or synthetic lipid, which is [Composition according to Claims 23 and 24;
characterized in that the neutral lipids are natural or synthetic lipids, which are]
zwitterionic or lacks an [lacking] ionic charge under physiological conditions[, chosen,
for example, from dioleoylphosphatidylethanolamine (DOPE),
oleylpalmitoylphosphatidylethanolamine (POPE), di-stearoyl, -palmitoyl,
-myristoylphosphatidylethanolamines and also the derivatives thereof which are
N-methylated 1 to 3 times, phosphatidylglycerols, diacylglycerols,
glycosyldiacylglycerols, cerebroside (such as in particular galactocerebrosides),
sphingolipids (such as in particular sphingomyelins) or asialogangliosides (such as in
particular asialoGM1 and GM2)].

26. The composition of Claim 22, wherein [Composition according to Claim 22,
characterized in that] said adjuvant is a compound involved [which is involved directly
or indirectly] in the condensation of the nucleic acid.

27. (Amended) The composition of Claim 26, wherein [Composition according to Claim 26, characterized in that] said adjuvant is derived, as a whole or in part, from a protamine, from a histone or from a nucleolin, and/or from a derivative thereof, or consists, as a whole or in part, of peptide units (KTPKKAKKP) (SEQ ID NO:1) and/or (ATPAKKAA) (SEQ ID NO:2), the number of units possibly ranging between 2 and 10, and possibly being repeated continuously or discontinuously.

28. (Amended) The composition of Claim 18, further comprising [Composition according to Claims 18 to 27, characterized in that it comprises] a vehicle which is pharmaceutically acceptable for an injectable formulation.

29. (Amended) The composition of Claim 18, further comprising [Composition according to Claims 18 to 27, characterized in that it comprises] a vehicle which is pharmaceutically acceptable for application to the skin and/or mucous membranes.

31. (Amended) Method for treating a [the] human or animal body, comprising the following steps:

- (1) contacting a [bringing the] nucleic acid [into contact] with a transfer agent as defined in Claim 1 [Claims 1 to 17, so as] to form a complex, and
- (2) contacting [bringing the] cells of the human or animal body [into contact] with the complex formed in (1).

32. (Amended) Method for transferring nucleic acids into cells, comprising
[characterized in that it comprises] the following steps:
(1) contacting a [bringing the] nucleic acid [into contact] with a transfer agent of Claim 1
[as defined, so as] to form a complex, and
(2) contacting [bringing] the cells [into contact] with the complex formed in (1).

33. (Amended) Method of Claim 32 for transferring nucleic acids into cells,
wherein [according to Claims 31 or 32, characterized in that] said transfer agent and/or
said nucleic acid are mixed beforehand with an adjuvant [one or more adjuvant(s) as
defined in Claims 22 to 27].